the combined opinions of many of the country's leading obstetricians. Since it was first offered to the public in July, 1938, there have been 2,700 copies supplied through that publication. In addition to the booklet, this service answers many letters a year in response to requests for special information.

The Metropolitan Life Insurance Company issues a forty-three page booklet, "Information for Expectant Mothers." They say that it has been compiled from the extensive literature of the United States Department of Labor and of the New York Maternity Center, and from pamphlets of the National Public Health Nursing Organization; and, although gathered by laymen, is authoritative in every detail. They feel that, in addition to helping the general program of public health, it saves them money in the conservation of lives.

The Prudential Insurance Company makes use of Doctor Bundeson's booklet in much the same way.

The free, or part-free clinics of larger cities are doing much to educate the charity patient. The Los Angeles Health Department's charity division last year cared for eighty home cases and three hundred hospital cases. In addition to well-organized literature, they are now instructing the patients by a series of moving pictures at the free clinics.

IN CONCLUSION

Certainly, all this instruction by laymen is doing much toward creating a higher standard of maternity care. It is valuable to the patient and, indirectly, to her doctor. It keeps the average physician aware of, and awake to his responsibility. We, as doctors, rather than make light of such popular literature, should encourage the public use of the materials at their command. It behooves us, in a way, to educate our patients during the period they are in our care. We should take time to learn as much as possible of each patient's personal psychology, and determine her likes and dislikes; to consider her demands for anesthesia, to learn her hopes and fears and, above all, to completely gain her confidence and dispel her fears. She should be treated not as just another case, but as the individual personality which she is.

3770 Twelfth Street.

THE PRESENT STATUS OF ARTIFICIAL FEVER IN THE TREATMENT OF SYPHILIS*

By NORMAN N. EPSTEIN, M.D.
San Francisco

ARTIFICIAL-FEVER therapy has been employed in the treatment of syphilis for over twenty years. During this period much has been done to evaluate its place in the management of the patient with this disease. While the beneficial effects of artificial-fever therapy are frequently striking, we have learned that it is not a panacea, and must be regarded simply as an addition to our armamentarium for use only under certain conditions. The limitations and hazards of this form of therapy have been pointed out very clearly. The purpose of this paper is to discuss the indications for artificial-fever therapy in the treatment of syphilis.

ARTIFICIAL-FEVER THERAPY

Artificial fever may be induced by any one of the following methods: the introduction into the patient of a parasitic disease which is usually accompanied by fever, such as malaria; the injection of a foreign protein; injections of chemical substances such as sulphur; electrical means such as the administration of diathermy or radiotherapy, or placing the patient in an electromagnetic field; and simple immersion of the individual in a hot bath, placing him in a heat cabinet, or wrapping him in blankets and adding an external source of heat.

There has been a tendency recently to employ the simpler methods for inducing artificial fever. Malaria is still the method of choice where a biologic method is used, and some form of radiant heat is preferred when a mechanical method is employed.

The value of each of the methods is undeniable, and each has its special indications. I have been more interested in mechanical methods because there is need for a form of artificial-fever therapy for the ambulatory patient. To meet this need we have developed a simple plan called the blanket method, which has been described in detail elsewhere.[1,2] We have found little difficulty in producing and controlling artificial fever by this method, but it requires an experienced staff and a well-equipped hospital. Artificial-fever therapy should be administered only in a hospital, and only with due consideration of its dangers. Under these conditions, the hazards of artificial-fever therapy are reduced to a minimum. During the past five years, we have given over three thousand such treatments. One death occurred in a very badly deteriorated paretic. The reader is referred to previous publications[1,2] concerning the indications, contraindications, hazards, and technique of inducing artificial fever.

RATIONALE OF ARTIFICIAL-FEVER THERAPY IN SYPHILIS

For centuries, heat has been used in various ways for the cure of disease and the alleviation of suffering. As in the case of many other medical discoveries, clinical experience preceded scientific explanation. Von Jauregg,[3] because he noted that patients insane with general paralysis occasionally became sane after some febrile episode, attempted to induce fever in his patients with similar conditions. After trying to produce fever artificially by many methods, he finally chose malaria as the most satisfactory. In 1918 he showed that artificially induced malaria for treatment of paresis produced beneficial results which were at times astonishing. Later, it was shown that comparable therapeutic results could be obtained by various other methods for inducing artificial fever, provided the temperature was elevated to a certain height and maintained at that height for a sufficient length of time. It became apparent to most workers that the essential factor in this form of therapy was

* From the Department of Dermatology of the University of California Medical School, and the Department of Dermatology and Syphilology of the Mount Zion Hospital, San Francisco.

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the elevation of temperature rather than the method by which it was produced.

The beneficial effects of artificial-fever therapy may result either from injury or destruction of the infecting parasite, or from increased resistance of the host against the parasite. It is probable that the various methods differ in the degree to which they produce these effects. It is interesting to note that artificial-fever therapy has been of value primarily in two infections, namely, syphilis and gonorrhea. In both of these diseases the infecting organisms are pathogenic only to the human host. When placed in an environment outside the body, they are easily destroyed. Another common characteristic of these two diseases is that they are usually afebrile. These facts indicate that the organisms may be more vulnerable to sudden changes within the host's body. A rapid elevation of temperature creates an environment which is not suited for the growth of these parasites.

Carpenter, Boak, aud Warren[4] demonstrated that the thermal death point of Treponema pallidum *in vitro* was 42 degrees C. (106.7 degrees F.) maintained for one hour; 41 degrees C. (105.8 degrees F.) for two hours; 40 degrees C. (104 degrees F.) for three hours; and 39 degrees C. (102.2 degrees F.) for five hours. Other workers have shown that experimental animals can be protected against successful inoculation with Treponema pallidum, and that syphilitic lesions can be sterilized of Treponema pallidum and caused to involute rapidly by elevating body temperature of the animals to heights within limits that can be attained safely in man. Bessemans and Thiry[5] demonstrated that, in human tissues, Treponema pallidum in primary and secondary syphilitic lesions can be rendered immotile and avirulent if the tissues are raised to a temperature of 42 degrees C. (106.7 degrees F.) for one hour, or 40 degrees C. (104 degrees F.) for two hours.

It is quite evident from *in vitro* studies, animal experimentation and studies on human tissues, that the Treponema pallidum can be either destroyed or markedly affected by temperatures between 40 degrees C. (104 dgrees F.) and 42 dgrees C. (106.7 degrees F.).

In addition to the direct effect of heat upon these organisms, artificial fever probably plays some part in stimulating tissue resistance.

ARTIFICIAL FEVER IN THE TREATMENT OF EARLY SYPHILIS

Inasmuch as temperatures that can be safely induced in man have such a profound effect upon Treponema pallidum, it is natural to ask, why not use this form of therapy in early syphilis and sterilize the individual of his parasites quickly? Considerable work has been done in the treatment of the early phase of syphilis with artificial fever, but the results have been unsatisfactory. Kerl,[6] between the years 1925 and 1929, observed 1,600 cases of early syphilis treated with short courses of arsphenamin and bismuth, combined with malarial therapy. He concluded that malarial therapy in early syphilis was of little curative value. Artificial fever produced by mechanical methods, when given alone, has failed uniformly in the treatment of early syphilis.

In 1935, we (Epstein and Cohen[2]) subjected thirty-three patients with primary and secondary syphilis to artificial-fever therapy without any other treatment. Although in 94 per cent of these cases the darkfield examinations were rendered negative and the lesions healed promptly with artificial fever, yet there was no evidence that the infection had been completely eradicated. In three patients there was recurrence promptly following cessation of the fever therapy, and in no patient was a positive blood Wassermann rendered negative.

At present, considerable experimental work is being done combining artificial fever produced mechanically with short courses of neoarsphenamin and bismuth. This procedure is highly experimental, and to me does not seem to offer a solution to the problem of early syphilis.

Probably the most important reason why fever therapy has failed to cure early syphilis lies in the fact that the human tissues do not heat up uniformly when subjected to artificial fever or during fevers of natural origin. Sampson[7] showed that during states of artificial fever there was a considerable variation between the temperature of the oral and rectal regions, as compared with the temperature of the venous blood, the subcutaneous tissues, the muscles, and the skin. The temperature of the venous blood remains 1 to 2 degrees centigrade below the oral temperature, and the temperature of the subcutaneous tissues and the exposed skin is also lower. Our inability to raise the temperature of all the tissues of the body to the thermal death point of the Treponema pallidum probably accounts for the failure of artificial fever to cure early syphilis.

ARTIFICIAL FEVER IN THE TREATMENT OF LATE SYPHILIS

At the present time, artificial-fever therapy, as applied to syphilis, has proved of definite value only in the treatment of the various forms of neurosyphilis. We have found it of little benefit in the management of patients with early syphilis, "Wassermann-fast" latent syphilis, and in the many other varieties of late syphilis. Artificial fever is limited in its use to the treatment of neurosyphilis, but never should be used as the only method of attack. In the treatment of resistant syphilis of the central nervous system, we should not depend upon any one method of therapy, but should be prepared to use every therapeutic agent at our command, according to the indications of the particular case. When artificial fever is induced by physical means, chemotherapy should be continued simultaneously with the fever therapy. Drug therapy should be given intensively and adequately, and in undiminished dosage. When artificial fever is induced by malarial inoculation, chemotherapy should follow the termination of the malarial paroxysms.

The results that one might expect to obtain in the treatment of the clinical forms of neurosyphilis are dependent not alone upon the therapeutic procedures applied, but also to a large extent upon the type of neurosyphilis being treated and the extent

of the damage that has been produced by the disease before therapy is instituted. It is well known that the meningovascular types of neurosyphilis respond very well to therapy. When treating the degenerative forms of neurosyphilis, such as paresis, taboparesis, and tabes dorsalis, the therapeutic response is frequently dependent upon the degree of degeneration present. Regardless of the method of therapy used, we would not expect to benefit the markedly deteriorated paretic; while, on the other hand, brilliant results may be obtained in the early paretic with a minimal amount of destruction of his cerebral cortex. In judging a given method it is very important, therefore, that these factors be considered carefully.

Artificial fever is indicated primarily for the treatment of general paresis and taboparesis. In these forms of neurosyphilis it should be instituted as soon as possible. In many cases this type of therapy is almost an emergency procedure as the degenerative process may progress rapidly.

We consider a course of pyrotherapy to consist of a total of fifty hours of fever, the temperature being maintained between 40 degrees C. (104 degrees F.) and 40.5 degrees C. (105 degrees F.). Ten weekly treatments are given, each consisting of five hours of maximum temperature. It is frequently necessary to give repeated courses of fever after six-month to yearly intervals.

In tabes dorsalis, artificial fever should be employed when the condition has not responded well to chemotherapy. It should be used when lightning pains or crises have been intractable. It is occasionally of value in the progressive optic atrophy of tabes.

Fever therapy is indicated in all other forms of neurosyphilis that prove resistant to drug therapy. In meningovascular, in diffuse cerebrospinal, and in asymptomatic neurosyphilis, fever therapy should be used only after drug therapy has been given an adequate trial.

RESULTS OF TREATMENT OF NEUROSYPHILIS WITH FEVER THERAPY

For several years we have combined fever therapy with drug administration, according to the indications given above, in our ambulatory clinic and private practice. In 1938, I reported the therapeutic results obtained in eighty-seven such patients.[8] The various forms of neurosyphilis were represented in the group. The clinical and serologic response was very satisfactory and compared favorably with those from other methods of fever therapy. A brief summary of the findings is as follows:

There were 17 cases of general paresis, 17 of taboparesis, 23 of tabes dorsalis, 20 of asymptomatic neurosyphilis, and 10 of acute meningovascular neurosyphilis.

The entire group had been under observation for an average of 37.7 months, 19.7 months before fever therapy, and 18.0 months after fever therapy.

Drug therapy, given throughout the period of observation, consisted mainly of the use of bismuth salicylate, neoarsphenamin, and tryparsamid.

General Paresis.—The spinal fluid Wassermann either reversed to negative or became less positive in 76.4 per cent of the seventeen cases with general paresis. The colloidal gold curve became normal or improved in 76.4 per cent.

In general, the clinical response paralleled the serologic findings. Seven patients obtained complete clinical remission, five were moderately improved, three showed slight improvement, and two no improvement.

Taboparesis.—The seventeen patients with taboparesis did not respond as well as did the group with general paresis. In 52.9 per cent, the spinal fluid Wassermann either reversed to negative or became less positive. The colloidal gold curve became normal in 11.8 per cent and improved in 70.5 per cent. In eight patients the clinical results were excellent, in eight moderate or slight improvement was noted, and one showed no improvement.

Tabes Dorsalis.—The spinal fluid Wassermann reversed to negative in 73.9 per cent of the twenty-three cases, and became less positive in 4.3 per cent. The colloidal gold curve became normal or improved in 60.2 per cent. The clinical effects did not parallel the serologic response, although many of these patients experienced considerable relief from their symptoms.

Asymptomatic Neurosyphilis. — In the twenty cases with this form of neurosyphilis, the spinal fluid Wassermann reversed to negative, and the colloidal gold curve became normal in 70 per cent and improved in 15 per cent. These findings are more significant because this group of patients had had an average of one and one-half years of drug therapy before fever therapy had been given.

Meningovascular Neurosyphilis. — There were ten cases in this group. The spinal fluid Wassermann reversed to negative or became less positive in 70 per cent, while the colloidal gold curve either became normal or improved in 90 per cent.

COMMENT

It was noted that, in the entire series of cases, the cell count was the most easily influenced element in the spinal fluid, becoming normal in 95 per cent.

The protein content of the spinal fluid was reduced to normal or improved in 74 per cent of the series.

Further observation of this group of patients and others will be necessary in order to confirm or modify the serologic and clinical results obtained. At present they are encouraging and indicate that this method of approach to the problem of the treatment of neurosyphilis is very satisfactory.

SUMMARY AND CONCLUSIONS

Artificial-fever therapy has a definite place in the management of the patient with neurosyphilis. It is of particular value in paresis and taboparesis, and is a helpful adjunct in the treatment of other forms of neurosyphilis that prove resistant to drug therapy. Our experience in the group of patients with asymptomatic neurosyphilis indicates that fever therapy may be of considerable value in preventing progression of the disease before late lesions appear.

Up to the present time, artificial-fever therapy without other therapy has been found to be unsatisfactory in the treatment of early syphilis. Certain investigative work is being conducted, combining artificial fever with drug therapy for cases of early syphilis. The value of this procedure has not been established.

We have found pyrotherapy unsatisfactory in the treatment of "Wassermann-fast" latent syphilis, and of all forms of late syphilis other than neurosyphilis.

The technical difficulties and hazards of inducing artificial fever have been eliminated to a large extent. This form of therapy should, however, be carefully controlled, and should be administered only by a thoroughly trained personnel and in an adequately equipped hospital.

The theoretical aspects of the rationale of artificial-fever therapy in syphilis have been discussed.

450 Sutter Street.

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SANTIAGO RAMÓN Y CAJAL*

By JOHN B. DOYLE, M. D.
Los Angeles

ALMOST a century ago there arose from the common people of Spain a character of such outstanding proportions and versatility as to warrant a place in history with Cervantes, Velasquez and Calderón de la Barca.

Santiago Ramón y Cajal was born at Petilla, in Aragon, on May 1, 1852. His father was a conscientious, ambitious, enterprising man who was not content to remain a "surgeon of the second class," and so, by dint of hard work and economies, he completed the course in medicine while burdened with an increasing family. From him Cajal inherited his physical and mental characteristics, including a will to power, determination, ambition and a splendid memory. Cajal's mother was a woman of fine character and great beauty. It was Cajal's regret that she did not transmit her physical characteristics to any of her children.

BOYHOOD DAYS

Like the majority of youngsters brought up in the country, Cajal was an outdoor enthusiast who, though shy, delighted in pranks. At an early age he began to collect birds and birds' eggs. Playing at war, he developed a science of ballistics, and even wrote a small treatise on lapidary strategy.

Formal education for Cajal began at 4 years of age. By 7 or 8 he was manifesting unusual interest and appreciable talent in both drawing and painting with water colors, to the disgust and dismay of his father, who wished that nothing might interfere with the classical education he had planned for him in preparation for a medical career. Before Cajal was 8 he was profoundly impressed by the return of Spanish troops from victories in Africa; and at that early age the germ of a sense of patriotism was awakened in him. A stroke of lightning, which killed a priest while he was ringing a bell in a belfry, seriously disturbed his faith in the working of a divine providence. On the other hand, he was greatly moved by an eclipse, which had been predicted by men who could not control lightning.

Life for Cajal, when between 10 and 13 years of age, was stormy. Bored by memorizing Latin and Greek, his obstinacy and defiance led to floggings. On one occasion he was deprived of a part of his food for five months and became greatly emaciated. In order to provide his son with a trade, if not a profession, his father, in desperation, apprenticed him to a barber. Cajal made friends in this environment. By writing poetry, for the barber's assistant, to a servant girl, he obtained music lessons. For music, however, he had no talent and made little progress. When he was apprenticed at a later date to a shoemaker, he soon became so adept that he was entrusted with work of the most fastidious nature. On being permitted to return to school, he resumed drawing, at which he excelled. This led to a very embarrassing incident when he caricatured a prominent teacher, whose injured egotism would not be soothed.

YOUNG MANHOOD

At 16 years of age Cajal's interest in photography was awakened. He was "astonished unspeakably" by manipulations for the production of a photogenic layer on wet collodion, and "stupefied" by the development of the latent image by pyrogallic acid. Later, he made important contributions to this art, including a work on color photography.

At 17 Cajal began the study of osteology. Bones for study were procured by father and son after dark from the local cemetery. Great was his parent's amazement and joy when his child manifested interest of high degree, a proficiency in drawing pictures of bones from all angles, and an astounding memory for anatomic details. For the ensuing

* Address of Section Chairman. Read before the Section on Neuropsychiatry of the California Medical Association at the sixty-eighth annual session, Del Monte, May 1–4, 1939.